Syntheses and Properties of Tetraaza-, Diaza-, Tetraoxa-, and Dioxa-metacyclophanes

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Metacyclophanes were prepared by cyclization reactions between bis(chloromethyl) compounds and piperazine, primary amines, or ethylene glycol. The ^1H nmr relaxation time (T_1) measurements indicated that the macrocycles feature the up and down motion of the aromatic units around the XCH_2Ar (X = N, O) methylene moieties as the axes. Metacyclophanes incorporating piperazine units showed high complexation ability for alkaline metal cations.

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Introduction.

Cyclophanes play a broad and prominent role in supramolecular chemistry. Although numerous papers concerning their syntheses and the properties of paracyclophanes have been reported [1], we noticed that few metacyclophanes designed for host moleclues have appeared in the literature except for the calixarenes [2].

The formation of the macrocycles is usually difficult because of the unfavorable activation entropy for the cyclizations. However, some cyclization reactions proceed efficiently and produce the macrocycles in satisfactory yields even without the template effect [3]. These efficient cyclization reactions may be due to the favorable positions of the reaction sites in the linear intermediate. Considering the easy preparation of the metacyclophanes such as the calixarenes, bisphenol-A and the phenol-formaldehyde dimer unit are a good choice as the building block of the metacyclophanes because of their structural resemblance to the calixarenes.

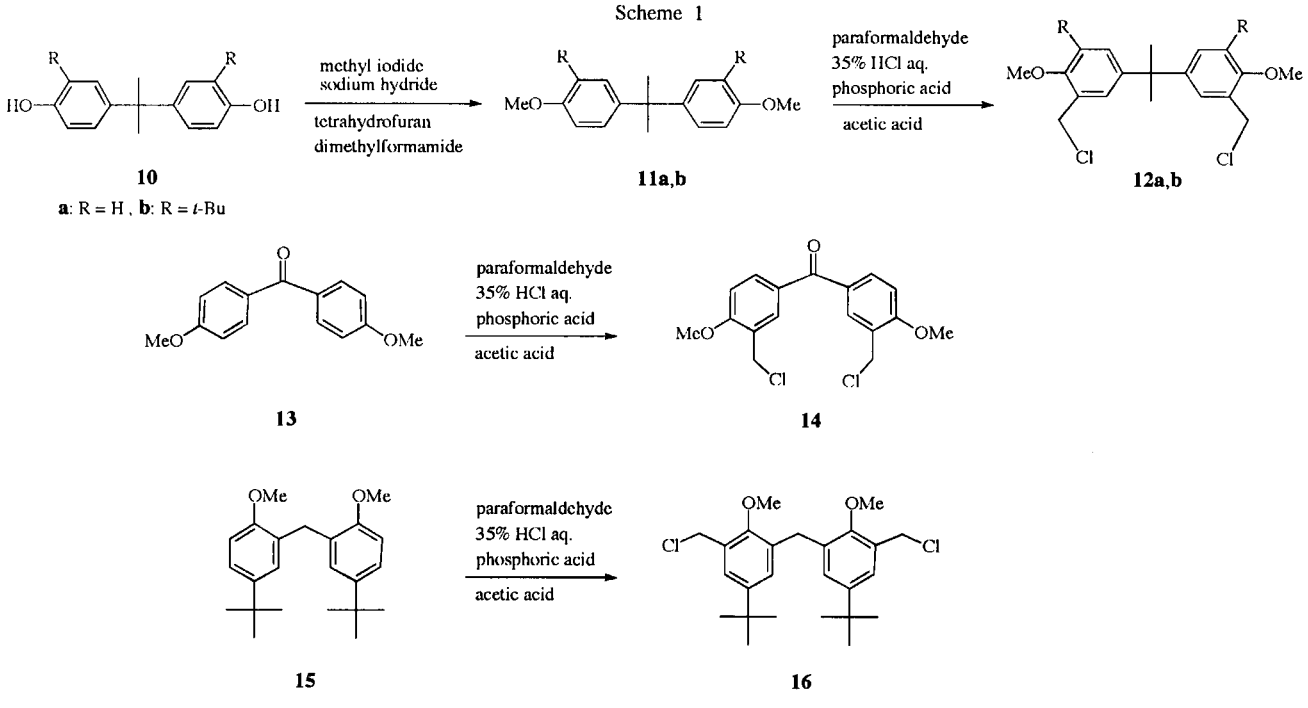
In this report we describe the preparation of the aza- and oxametacyclophanes incorporating the bisphenol-A unit and phenol-formaldehyde dimer moiety, and their molecular mobilities and complexation abilities for alkaline metal cations.

Results and Discussion.

Syntheses of the Metacyclophanes.

The tetraazametacyclophanes (**1a**) were prepared by the cyclization reactions of piperazine with the bis(chloromethyl) compound (**12a**), which was derived from the

Scheme 1



10
a: R = H, **b**: R = *t*-Bu

11a,b

12a,b

13

14

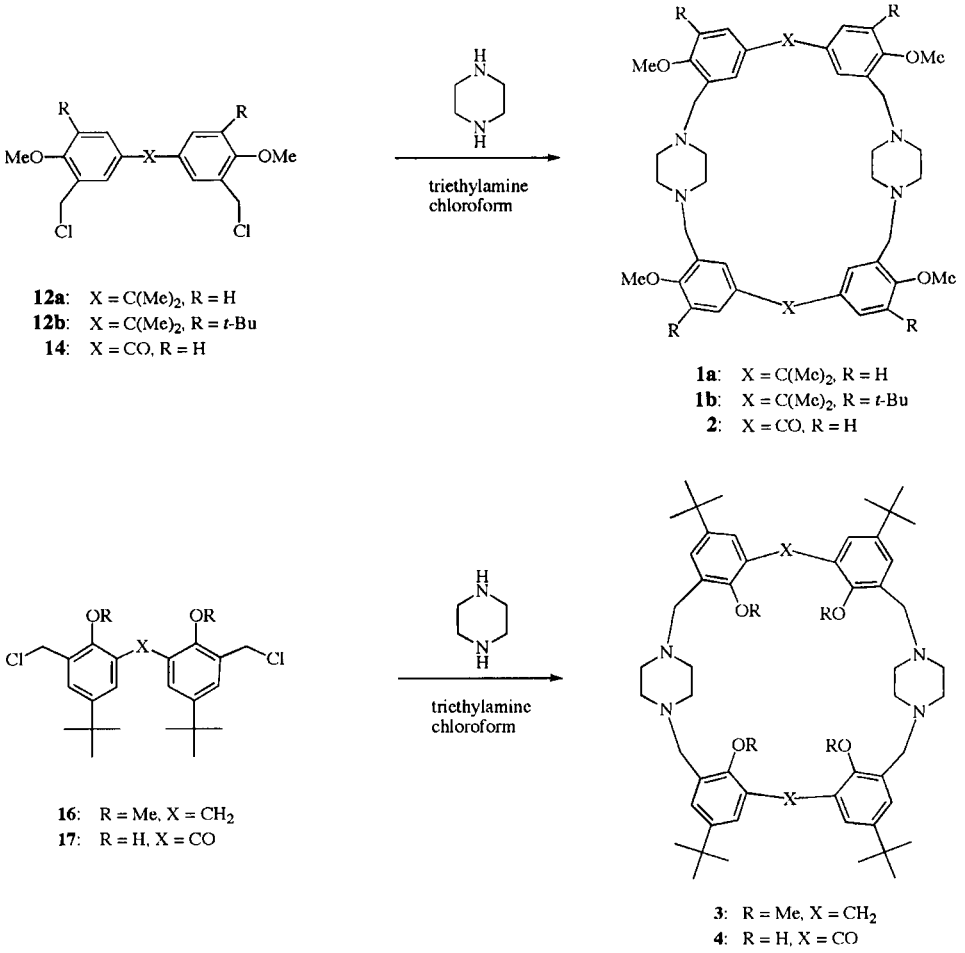
15

16

chloromethylation of the corresponding bisphenol-A derivative (**10a**), in the presence of triethyl amine in chloroform in 94% yield. Analogous reactions using **12b**, **14**, **16**, and **17** instead of **12a** also gave the corresponding 2:2 macrocycles (**1b**, **2**, **3**, and **4**) in 72, 68, 75, and 82% yields, respectively. Interestingly, these reactions selectively gave the 2:2 macrocycles in high yields, without using metal ions as a template.

phanes from the reactions between the bis(chloromethyl) compounds (**12**, **14**, and **16**) having a methoxy group with the primary amines, but we did not obtain macrocycles only polymeric materials. Therefore, we used **19**, which contains hydroxy groups instead of methoxy groups, as the bis(chloromethyl) compounds. The cyclization reaction of **19** with benzylamine in the presence of sodium carbonate gave the 2:2 macrocycle (**9a**) in 40% yield.

Scheme 2



12a: X = C(Me)$_2$, R = H
12b: X = C(Me)$_2$, R = *t*-Bu
14: X = CO, R = H

1a: X = C(Me)$_2$, R = H
1b: X = C(Me)$_2$, R = *t*-Bu
2: X = CO, R = H

16: R = Me, X = CH_2
17: R = H, X = CO

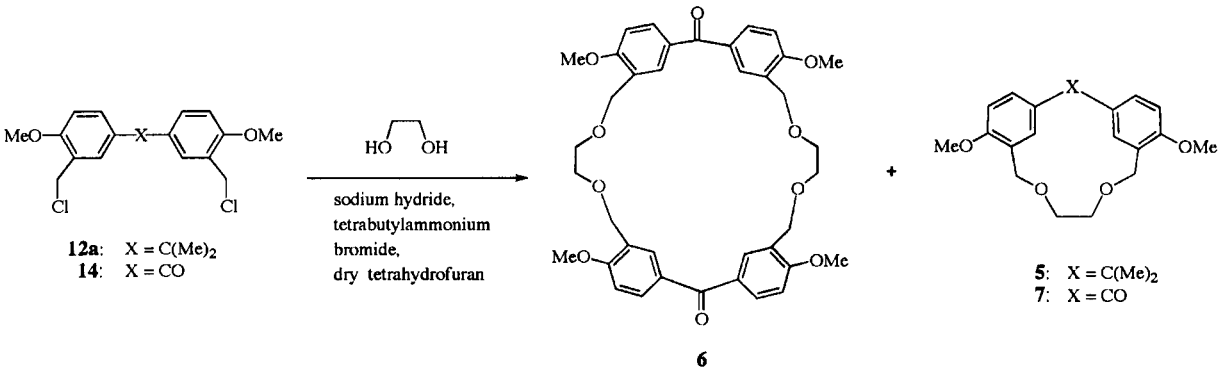
3: R = Me, X = CH_2
4: R = H, X = CO

Although we also carried out the formation of the tetraoxametacyclophanes using similar cyclization reactions between **12a** with ethylene glycol in the presence of sodium hydride in dry tetrahydrofuran, we obtained only the 1:1 macrocycle (**5**), dioxametacyclophane, in 44% yield. Using **14** instead of **12a**, the 2:2 and 1:1 macrocycles (**6** and **7**) were produced in 12 and 34% yields, respectively. The reaction of **16** with ethylene glycol gave the 2:2 macrocycle (**8**) in only a 3% yield.

We examined the formation of the diazametacyclo-

Analogous reactions using chiral amines such as *L*-valine methylester, *L*-tyrosine methylester, and (*R*)-phenethyl amine instead of benzyl amine also afforded the corresponding 2:2 macrocycles (**9b-d**) in 15, 32, and 50% yields, respectively. When these reactions were carried out in the presence of triethyl amine in chloroform, we did not obtain macrocyclic compounds except for polymeric materials. Therefore, the formation of the 2:2 macrocycles (**9**) may be related to the template effect of the metal cation.

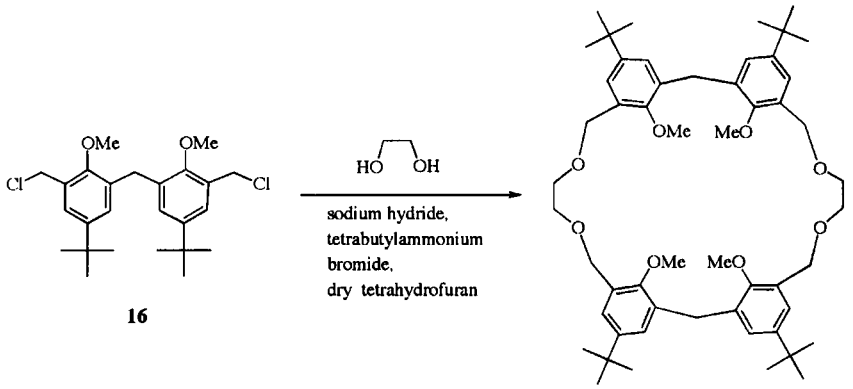
Scheme 3



12a: X = $C(Me)_2$
14: X = CO

6

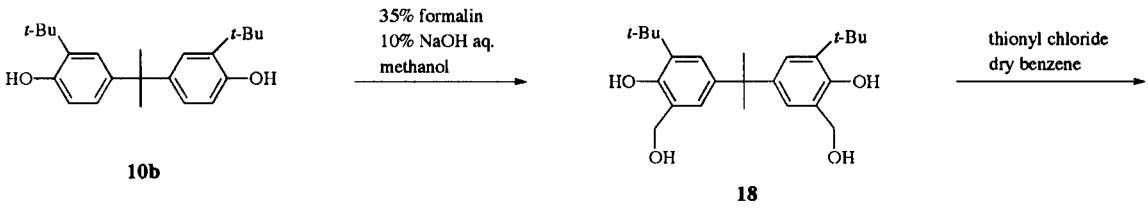
5: X = $C(Me)_2$
7: X = CO



16

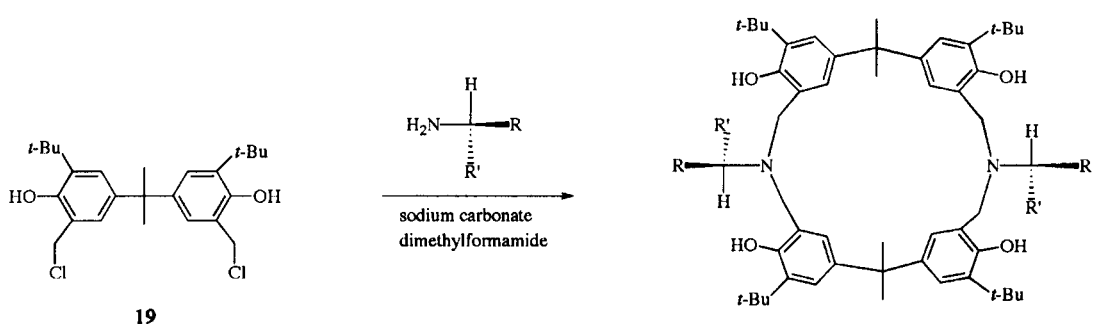
8

Scheme 4



10b

18



19

9a: R = Ph, R' = H
9b: R = CO_2Me, R' = $CH(Me)_2$
9c: R = CO_2Me, R' = CH_2Ph
9d: R = Me, R' = Ph

Structures of the Metacyclophanes.

The structures of the metacyclophanes (**1-9**) were elucidated on the basis of their spectral data, especially the nmr spectroscopy.

In the ^{1}H nmr spectra of the macrocycles (**1-9**) at ambient temperature, the XCH_2Ar (X = N, O) methylene signals were observed as a singlet due to the conformational flexibility of the ring system. Therefore, we carried out variable temperature ^{1}H nmr experiments. The methylene signals of the macrocycles (**1-8**, and **9d**) resulted in signal broadening at low temperature, but did not split even at -60° in deuteriochloroform. In contrast, the diazametacyclophanes (**9a**, **9b**, and **9c**) showed a different behavior during the variable temperature ^{1}H nmr experiments. At 55°, the ^{1}H nmr spectrum of **9a** contains one *tert*-butyl signal, two methylene signals, and two phenol ring proton signals indicating that the four phenols in the cyclophane moiety are equivalent on the nmr time scale. The spectra of **9b** and **9c** also contain one *tert*-butyl signal and two phenol proton signals. At -60°, the spectrum of **9a** contains two *tert*-butyl signals, three pairs of doublets arising from the methylene protons, and four phenol proton signals, indicating that the protons of each phenol unit in the bisphenol-A moiety are not equivalent on the nmr time scale (Figure 1). Interestingly, the chiral macrocycles (**9b** and **9c**) result in more complex signals at low temperature. Their ^{1}H nmr spectra at low temperature display four *tert*-butyl signals, four pairs of doublets due to the $ArCH_2N$ methylene protons, and eight phenol protons, indicating that all the phenol units in the macrocycles are nonequivalent on the nmr time scale (Figure 2).

Molecular Mobility of the Macrocycles.

Measurements of ^{1}H nmr relaxation times (T_1) were made to gain a deeper insight into the dynamic behavior of the macrocycles in solution [4]. Therefore, we carried out measurements of ^{1}H nmr relaxation time by using the inversion recovery method at 24° in deuteriochloroform and the results are shown in Figure 3. The T_1 measurements of the 2:2 macrocycles (**1**, **2**, **3**, **4**, **6**, and **8**) show that the T_1 values of the XCH_2Ar (X = N, O) methylene protons are relatively small. This means that the motion of the aromatic units is characterized by the up and down motions around the methylene moieties as the axes. Comparing the molecular motions between the macrocycles (**1**) incorporating the bisphenol-A units and the macrocycles (**3** and **4**) incorporating the phenol-formaldehyde dimer moieties, the bisphenol-A unit suppressed the flexbility of the macrocycles to a greater degree.

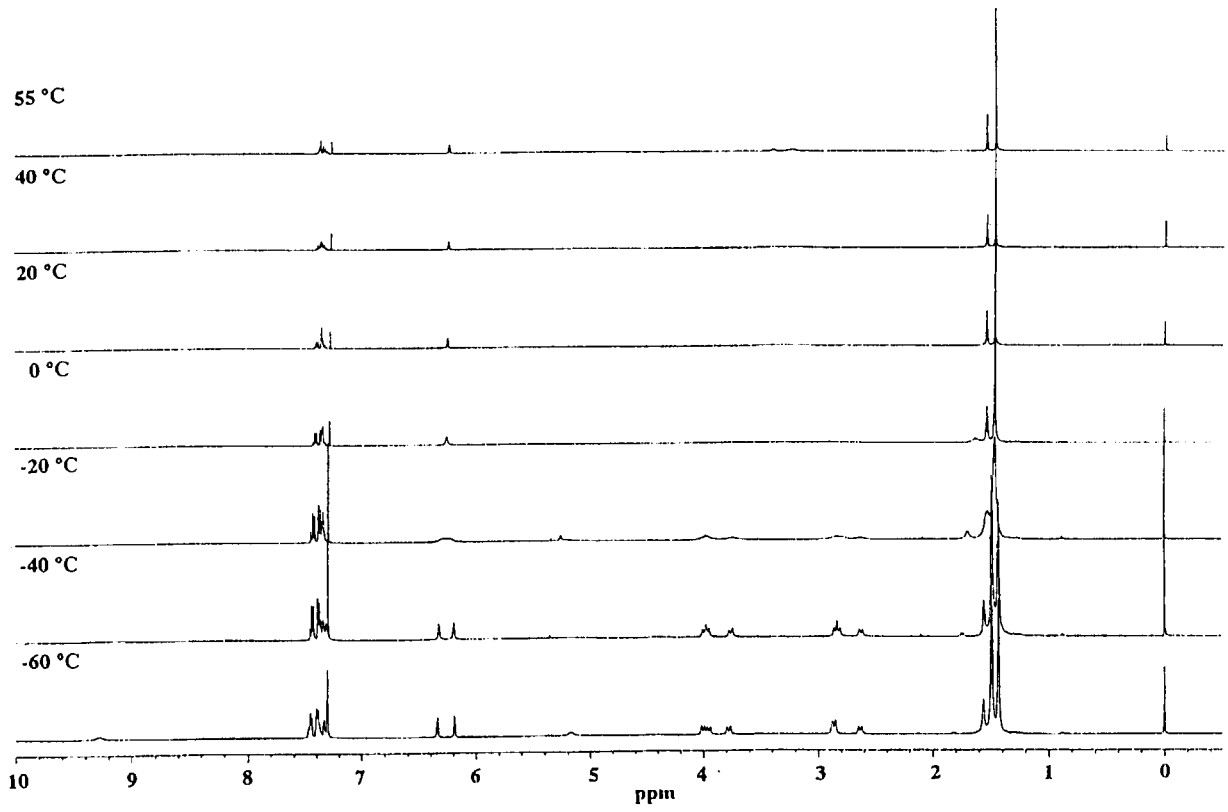


Figure 1. Variable temperature ^{1}H nmr spectra of the macrocycle (**9a**) in deuteriochloroform at 500 MHz.

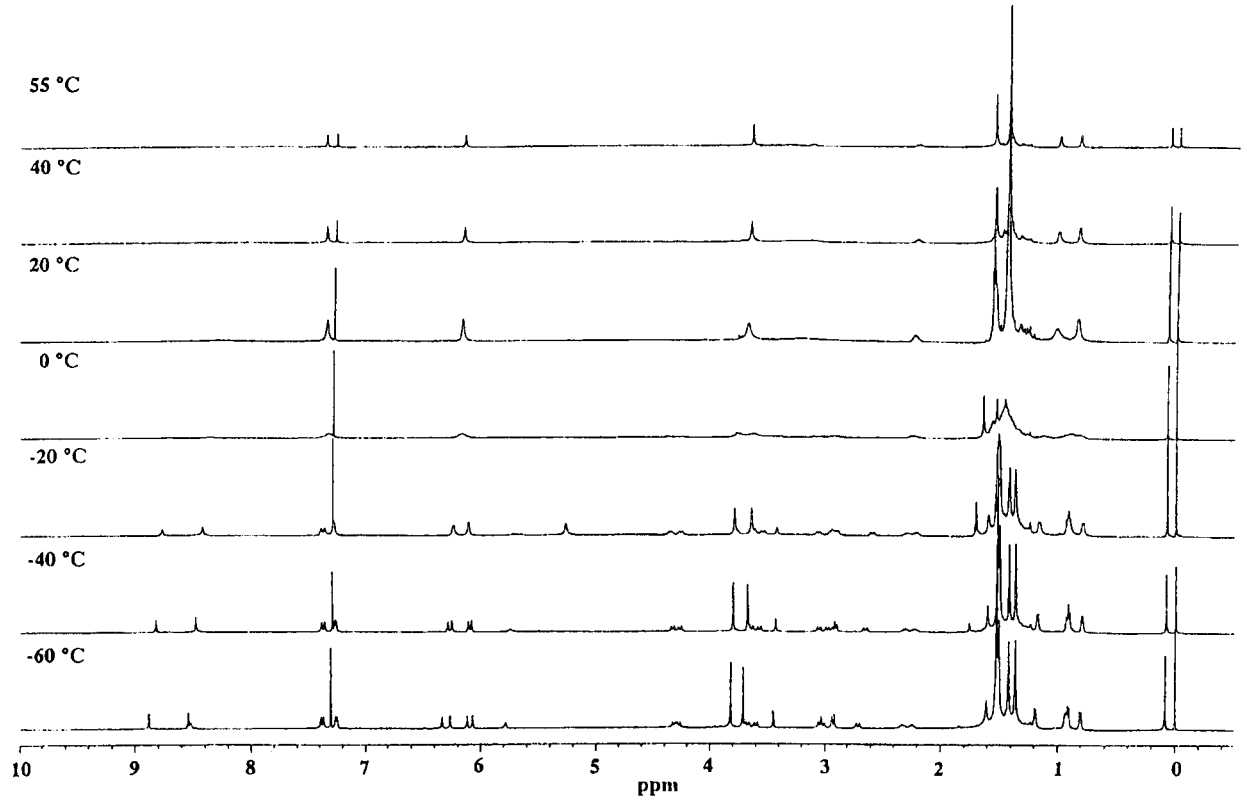


Figure 2. Variable temperature ^{1}H nmr spectra of the macrocycle (**9b**) in deuteriochloroform at 500 MHz.

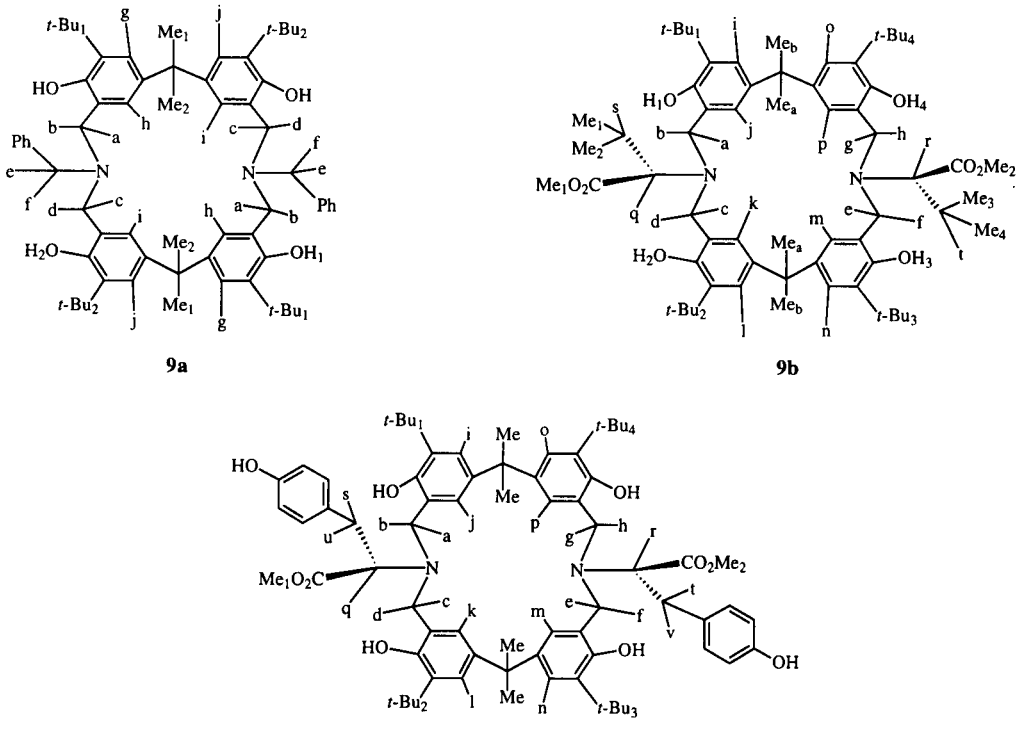


Figure 3. Assignments of the protons of the macrocycles (**9a**, **9b**, and **9c**) using cosy and roesy spectra in deuteriochloroform at low temperature.

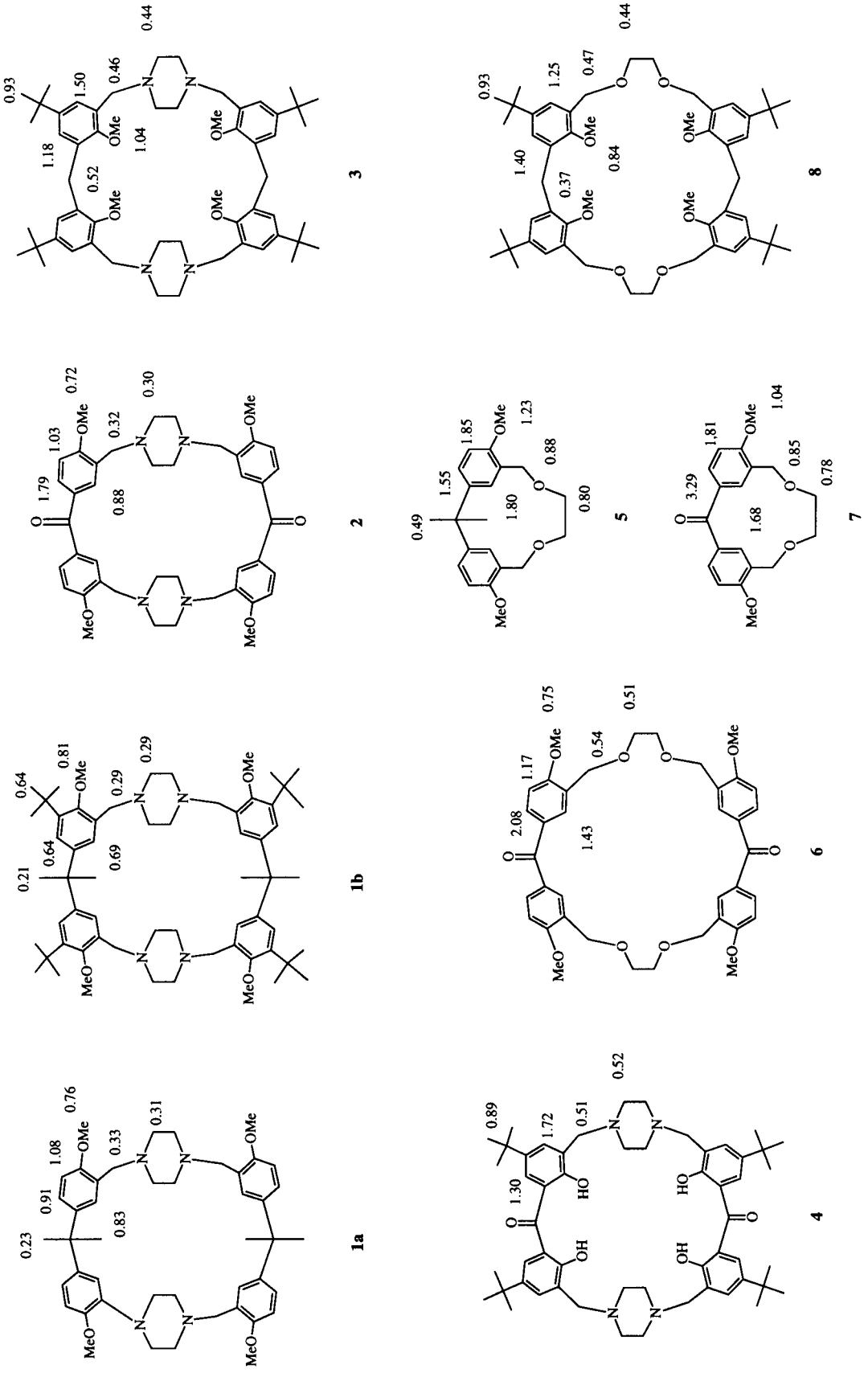


Figure 4. T_1 Values [second] of the metacyclophanes (**1-8**).

Complexation Ability for Alkaline Metal Cations.

The extraction ability of the metacyclophanes (**1-9**) towards alkaline metal cations was examined using Pedersen's extraction method [5]. Table 1 summarizes these results. The tetraazametacyclophanes (**1-4**) having piperazine units showed a high extractability, but low selectivity for these cations. On the other hand, the extraction ability of the diazametacyclophanes (**9a** and **9b**) was lower than that of the tetraazametacyclophanes. In contrast, the oxametacyclophanes (**5-8**) did not show any extraction ability for the cations. From these results, the piperazine unit of the macrocycles is considered to play an important role in the extraction of the alkaline metal cations. In **3**, the ^{1}H nmr chemical shifts of the methylene protons of the piperazine unit and of the $ArCH_2N$ in the presence of the cations shift to a lower magnetic field (δ_{NCH2} 2.52 ppm and δ_{ArCH2N} 3.56 ppm in the absence of Na^+, δ_{NCH2} 2.76 ppm and δ_{ArCH2N} 3.73 ppm in the presence of Na^+) , which is attributed to the electron-withdrawing nature of the cation.

Table 1

Extraction of Alkaline Metal Picrates with Macrocycles

Macrocycles	Extractability (%)				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	88	93	93	93	89
1b	95	96	96	96	95
2	76	82	81	76	73
3	99	99	99	99	99
4	69	67	64	71	48
5	0	1	1	0	1
6	1	1	2	2	1
7	1	1	1	2	2
8	0	0	0	0	0
9a	4	5	3	4	3
9b	10	11	12	12	11

Conclusion.

We synthesized the tetra- and di-azametacyclophanes by the 2:2 cyclization reactions between bis(chloromethyl) compounds and piperazine or primary amines in good yields. In contrast, the tetraoxametacyclophanes were not obtained or were formed in very low yields. The ^{1}H nmr relaxation time measurements of the macrocycles revealed the up and down motions of the aromatic units around the methylene moieties as axes. The tetraazametacyclophanes having piperazine units showed a high extractability for alkaline metal cations, but did not show good selectivity for the cations.

EXPERIMENTAL

Melting points were measured by Yanagimoto micro melting point apparatus and were uncorrected. The ^{1}H and ^{13}C nmr spectra were measured with Varian INOVA 500 or Mercury 200 spectrophotometers, using tetramethylsilane as an internal standard reference. The ir spectra were taken on Horiba FT-200 spectrophotometer. The fab- and ei-mass spectra were recorded on a JEOL JMS AX-505HA spectrometer. Column chromatography was performed using silica gel (Kieselgel 60, 63-200 μm, 70-230 mesh, Merck) or activated alumina (200 mesh, Wako). All chemicals were reagent grade and were used without further purification. Compounds (**10a** and **13**) were purchased from Tokyo Kasei Industry and Kanto Chemical Co., respectively. Compounds (**10b** [6], **11a** [7], **12a** [7], **15** [8], **17** [9]) were prepared according to the literature.

1-(*tert*-Butyl)-5-(1-(3-*tert*-butyl)-4-methoxyphenyl)isopropyl)-2-methoxybenzene (**11b**).

A mixtute of **10b** (39.7 g, 0.12 mole), sodium hydride (28.8 g, 1.20 moles), dry tetrahydrofuran (170 ml), and dry dimethyl formamide (60 ml) was stirred at room temperature for 1 hour. To the solution was added methyl iodide (37.3 ml, 0.60 mole) over 2 hours at room temperature. After the addition was completed, the mixture was heated at 60° for 5 hours. After cooling to room temperature, sodium hydride was quenched by methanol. To the mixture was added water (200 ml) and 10% HCl aqueous solution (100 ml), and then the mixture was extracted with chloroform (100 ml) 5 times. The organic layer was washed with 10% sodium thiosulfate aqueous solution (100 ml) 2 times and water (200 ml) until *p*H 7, and then dried over anhydrous sodium sulfate. Removal of chloroform gave pale brown solid, which was recrystallized from ethyl acetate to give **11b** (40.6 g, 94% yield) as colorless crystals, mp 106-107°; ir (chloroform): 2970, 1600, 1500, 1470, 1400, 1360, 1300, 1240, 1180, 1100, 1030 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.33 (s, 18H, *t*-Bu x 2), 1.67 (s, 6H, Me x 2), 3.82 (s, 6H, OMe x 2), 6.78 (d, 2H, aromatic protons, J = 8.5 Hz), 7.06 (dd, 2H, aromatic protons, J = 2.0, 8.5 Hz), 7.16 (d, 2H, aromatic protons, J = 2.0 Hz); ^{13}C nmr (deuteriochloroform): δ 29.8, 31.2, 34.9, 42.0, 54.9, 110.7, 124.8, 125.4, 137.1, 142.3, 156.2; ei-ms (70 eV): m/z 368 $(M)^+$.

Anal. Calcd. for $C_{25}H_{36}O_2$: C, 81.45; H, 10.54. Found: C, 81.47; H, 9.84.

General Procedure for the Preparation of Bis(chloromethyl) Compounds (**12b**, **14**, and **16**).

To a mixture of **11b**, **13**, or **15** (68 mmoles), paraformaldehyde (19.7 g, 680 mmoles), 35% hydrochloride aqueous solution (57 ml), and acetic acid (400 ml) was added phosphoric acid (18 ml) at 80° over 15 minutes, and then the mixture was heated (at 90° for 5 hours for **12b**, at 95° for 10 hours for **14**, at 80° for 4 hours for **16**). After cooling to room temperature, the mixture was poured into ice and extracted with chloroform (200 ml) 3 times. The organic layer was washed with water until *p*H 7, and dried over anhydrous sodium sulfate. Removal of chloroform by rotary evaporator gave a brown oily residue, which was subjected to column chromatography on silica gel (chloroform:hexane, 1:4 for **12b** and **14**, chloroform for **16** as an eluent) to give the corresponding bis(chloromethyl) compound as colorless crystals.

1-(*tert*-Butyl)-5-(1-(5-(*tert*-butyl)-3-(chloromethyl)-4-methoxyphenyl)isopropyl)-3-(chloromethyl)-2-methoxybenzene (**12b**).

The yield of **12b** was 40% as colorless crystals, mp 101-102°; ir (potassium bromide): 3018, 2962, 2930, 2867, 1600, 1477, 1430, 1359, 1259, 1234, 1218, 1160, 1112, 1001 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.31 (s, 18H, *t*-Bu x 2), 1.66 (s, 6H, Me x 2), 3.89 (s, 6H, OMe x 2), 4.66 (s, 4H, $ArCH_2Cl$ x 2), 7.07 (d, 2H, aromatic protons, J = 2.0 Hz), 7.19 (d, 2H, aromatic protons, J = 2.0 Hz); ^{13}C nmr (deuteriochloroform): δ 30.9, 31.0, 35.3, 42.2, 42.6, 62.8, 126.9, 127.9, 130.4, 142.2, 145.5, 155.8; ei-ms (70 eV): m/z 465 $(M)^+$.

Anal. Calcd. for $C_{27}H_{38}Cl_2O_2$: C, 69.67; H, 8.23. Found: C, 70.09; H, 9.02.

Di(3-(chloromethyl)-4-methoxyphenyl)ketone (**14**).

The yield of **14** was 74% as colorless crystals, mp 150-152°; ir (potassium bromide): 3018, 2962, 2930, 2867, 1600, 1477, 1430, 1359, 1259, 1234, 1218, 1160, 1112, 1001 cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.96 (s, 6H, OMe x 2), 4.67 (s, 4H, $ArCH_2Cl$ x 2), 6.96 (d, 2H, aromatic protons, J = 8.5 Hz), 7.88 (dd, 2H, aromatic protons, J = 2.0, 8.5 Hz), 7.85 (d, 2H, aromatic protons, J = 2.0 Hz); ^{13}C nmr (deuteriochloroform): δ 41.1, 55.9, 110.1, 125.8, 130.3, 132.7, 132.8, 160.6, 193.6; fab-ms: m/z 339 $(M+H)^+$.

Anal. Calcd. for $C_{17}H_{16}Cl_2O_3$, C, 60.19; H, 4.75. Found: C, 59.84; H, 4.60.

5-(*tert*-Butyl)-1-((5-(*tert*-butyl)-3-(chloromethyl)-2-methoxyphenyl)methyl)-3-(chloromethyl)-2-methoxybenzene (**16**).

The yield of **16** was 96% yield as colorless crystals, mp 91-92°; ir (potassium bromide): 2950, 1600, 1480, 1460, 1270, 1260, 1210, 1100, 1010, 1000 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.23 (s, 18H, *t*-Bu x 2), 3.80 (s, 6H, OMe x 2), 4.07 (s, 2H, $ArCH_2Ar$), 4.69 (s, 4H, $ArCH_2Cl$ x 2), 7.03 (d, 2H, aromatic protons, J = 2.4 Hz), 7.28 (d, 2H, aromatic protons, J = 2.4 Hz); ^{13}C nmr (deuteriochlorofrom): δ 29.7, 31.3, 34.3, 41.8, 61.9, 126.0, 128.8, 130.1, 133.2, 147.1, 154.5; ei-ms (70 eV): m/z 676 $(M)^+$.

Anal. Calcd. for $C_{25}H_{34}Cl_2O_2$: C, 68.64; H, 7.83. Found: C, 68.81; H, 7.98.

General Procedure for the Preparation of Tetraazametacyclophanes (**1a**, **1b**, **3**, and **4**).

To a solution of triethyl amine (1.65 ml, 12 mmoles) in chloroform (200 ml) were added a solution of bis(chloromethyl) compound (**12**, **16**, or **17**) (3.0 mmoles) in chloroform (50 ml) and a solution of piperazine (0.26 g, 3.0 mmoles) in chloroform (50 ml) at 20° over 7 hours under nitrogen atmosphere. After the addition was complete, the mixture was allowed to stir at 30° for 24 hours, and then the reaction mixture was washed with water 3 times and dried over anhydrous sodium sulfate. Removal of chloroform gave a brown oily residue, which was subjected to activated alumina (chloroform for **1a**, **3**, and **4**; chloroform:methanol, 50:1 for **1b** as an eluent) to give 2:2 macrocycle as colorless crystals.

1,15,18,32-Tetraaza-4,12,21,29-tetramethoxy-8,8,25,25-tetramethylheptacyclo[30.2.2.$2^{15,18}$.$1^{3,7}$.$1^{9,13}$.$1^{20,24}$.$1^{26,30}$]-dotetraconta-3(39),4,6,9(10),11,13(40),20(41),21,23,26(27),28,30(42)-dodecaene (**1a**).

The yield of **1a** was 94% yield as colorless crystals, mp 195° (decomp); ir (potassium bromide): 2964, 2827, 2804, 1605, 1498, 1462, 1302, 1244, 1136, 1109, 1032, 1011, 808 cm^{-1}; ^1H nmr (deuteriochloroform) : δ 1.64 (s, 12H, Me x 4), 2.31 (br s, 16H, methylene protons of piperazine), 3.45 (s, 12H, OMe x 4), 3.76 (s, 8H, $ArCH_2N$ x 4), 6.75 (d, 4H, aromatic protons, J = 8.6 Hz), 7.05 (d, 4H, aromatic protons, J = 2.3 Hz), 7.16 (dd, 4H, aromatic protons, J = 2.3, 8.6 Hz); ^{13}C nmr (deuteriochloroform): δ 30.7, 41.4, 52.8, 55.5, 56.1, 109.9, 125.1, 125.3, 129.8, 142.7, 155.6; fab-ms: m/z 733 $(M+H)^+$.

Anal. Calcd. for $C_{46}H_{60}N_4O_4$ 4(H_2O): C, 68.63; H, 8.51; N, 6.96. Found: C, 68.05; H, 8.47; N, 6.21.

1,15,18,32-Tetraaza-4,12,21,29-tetramethoxy-8,8,25,25-tetramethyl-5,11,22,28-tetrakis(*tert*-butyl)heptacyclo-[30.2.2.$2^{15,18}$.$1^{3,7}$.$1^{9,13}$.$1^{20,24}$.$1^{26,30}$]dotetraconta-3(39),4,6,9(10),11,13(40),20(41),21,23,26(27),28,30(42)-dodecaene (**1b**).

The yield of **1b** was 72% yield as colorless crystals, mp 253-254°; ir (potassium bromide): 2960, 2873, 2804, 1600, 1473, 1429, 1359, 1303, 1224, 1137, 1012 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.33 (s, 36H, *t*-Bu x 4), 1.65 (s, 12H, Me x 4), 2.30 (br s, 16H, methylene protons of piperazine), 3.39 (s, 8H, $ArCH_2N$ x 4), 3.72 (s, 12H, OMe x 4), 7.08 (d, 4H, aromatic protons, J = 2.5 Hz), 7.11 (d, 4H, aromatic protons, J = 2.5 Hz); ^{13}C nmr (deuteriochloroform): δ 30.4, 31.2, 35.2, 42.1, 53.0, 56.8, 62.3, 123.5, 127.8, 130.6, 141.2, 145.2, 156.1; ei-ms (70 eV): m/z 956 $(M)^+$.

Anal. Calcd. for $C_{62}H_{92}N_4O_4$ 2H_2O: C, 74.96; H, 9.74; N, 5.64. Found: C, 74.57; H, 10.17; N, 5.49.

1,15,18,32-Tetraaza-39,40,41,42-tetramethoxy-5,11,22,28-tetrakis(*tert*-butyl)heptacyclo[30.2.2.$2^{15,18}$.$1^{3,7}$.$1^{9,13}$.$1^{20,24}$.$1^{26,30}$]-dotetraconta-3(39),4,6,9(10),11,13(40),20(41),21,23,26(27),28,30(42)-dodecaene (**3**).

The yield of **3** was 75% yield as colorless crystals, mp 168-173°; ir (chloroform): 2940, 1470, 1450, 1350, 1200, 1000 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.21 (s, 36H, *t*-Bu x 4), 2.55 (s, 16H, methylene protons of piperazine), 3.58 (s, 8H, $ArCH_2N$ x 4), 3.73 (s, 12H, OMe x 4), 4.06 (s, 4H, $ArCH_2Ar$ x 2), 6.92 (d, 4H, aromatic protons, J = 1.2 Hz), 7.35 (d, 4H, aromatic protons, J = 1.2 Hz); ^{13}C nmr (deuteriochloroform): δ 31.3, 31.4, 34.2, 53.2, 57.2, 61.4, 125.9, 126.8, 130.2, 133.0, 146.1, 155.0; ei-ms (70 eV): m/z 900 $(M)^+$.

Anal. Calcd. for $C_{58}H_{84}N_4O_4$ 2.5(H_2O): C, 73.61; H, 9.47; N, 5.92. Found: C, 73.43; H, 9.45; N, 5.98.

1,15,18,32-Tetraaza-39,40,41,42-tetrahydroxy-5,11,22,28-tetrakis(*tert*-butyl)heptacyclo[30.2.2.$2^{15,19}$.$1^{3,7}$.$1^{9,13}$.$1^{20,24}$.$1^{26,30}$]-dotetraconta-3(39),4,6,9(10),11,13(40),20(41),21,23,26(27),28,30(42)-dodexaene-8,25-dione (**4**).

The yield of **4** was 82% yield as colorless crystals, mp 223-226°; ir (chlorofrom): 2960, 1620, 1600, 1480, 1455, 1360 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.24 (s, 36H, *t*-Bu x 9), 2.65 (s, 16H, methylene protons of piperazine), 3.73 (s, 8H, $ArCH_2N$ x 4), 7.31 (s, 4H, aromatic protons, J = 2.5 Hz), 7.34 (s, 4H, aromatic protons, J = 2.5 Hz), 12.05 (br s, 4H, OH x 4); ^{13}C nmr (deuteriochloroform): δ 31.4, 34.0, 52.6, 58.8, 60.4, 122.2, 123.3, 127.5, 131.6, 140.7, 156.5, 202.4; fab-ms: m/z 873 $(M+H)^+$.

Anal. Calcd. for $C_{54}H_{72}N_4O_6$ H_2O: C, 72.77; H, 8.37; N, 6.29. Found: C, 72.46; H, 8.38; N, 5.85.

Synthesis of 1,5,18,32-tetraaza-4,12,21,29-tetramethoxyheptacyclo[30.2.2.2^{15,18}.1^{3,7}.1^{9,13}.1^{20,24}.1^{26,30}]dotetraconta-3(39),4,6,9(10),11,13(40),20(41),21,23,26(27),28,30(42)-dodecaene-8,25-dione (**2**).

To a suspension of sodium carbonate (1.66 g, 12 mmoles) in dry dimethylformamide (200 ml) were added a solution of **14** (1.04 g, 6.0 mmoles) in dry dimethylformamide (50 ml) and a solution of piperazine (0.52 g, 6.0 mmoles) in dimethylformamide (50 ml) at 70° over 5 hours under nitrogen atmosphere. After the addition was complete, the mixture was further heated at 70° for 10 hours. Removal of dimethylformamide under reduced pressure gave a brown oily residue, which was dissolved with chloroform. The solution was washed with water and dried over anhydrous sodium sulfate. Removal of chloroform gave a brown solid, which was recrystallized from dichloromethane to give **2** (0.59 g, 28% yield) as colorless crystals, mp 172° (decomp); ir (potassium bromide): 2950, 2800, 1640, 1600, 1500, 1460, 1320, 1260, 1120, 1130, 760 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.51 (br s, 16H, methylene protons of piperazine), 3.62 (s, 8H, ArCH$_2$N x 4), 3.88 (s, 12H, OMe x 4), 6.98 (d, 4H, aromatic protons, J = 8.5 Hz), 7.67 (d, 4H, aromatic protons, J = 2.0 Hz), 7.87 (dd, 4H, aromatic protons, J = 2.0, 8.5 Hz); ^{13}C nmr (deuteriochloroform): δ 52.5, 55.7, 55.8, 110.6, 124.4, 130.0, 131.0, 134.2, 161.3, 194.4; fab-ms: m/z 704 (M+H)$^+$.

Anal. Calcd. for C$_{42}$H$_{48}$N$_4$O$_6$ 3/2(H$_2$O): C, 68.93; H, 7.02; N, 7.66. Found: C, 69.07; H, 6.74; N, 7.68.

General Procedure for the Preparation of Dioxa- (**5** and **7**) and Tetraoxametacyclophanes (**6** and **8**).

To a mixture of ethylene glycol (0.31 g, 5.0 mmoles), sodium hydride (0.30 g, 28 mmoles), tetrabutylammonium bromide (0.16 g, 0.50 mmole), and dry tetrahydrofuran (20 ml) was added a solution of the bis(chloromethyl) compound (**12a**, **14**, or **16**) (5.0 mmoles) in dry tetrahydrofuran (50 ml) at 60° over 3 hours. After the addition was complete, the mixture was further heated at 60° for 7 hours. After removal of the insoluble materials by filtration, condensation of the filtrate gave a brown oily residue, which was dissolved with chloroform. The solution was washed with water and dried over anhydrous sodium sulfate. Removal of chloroform gave a brown oily residue, which was subjected to column chromatography on silica gel using ethyl acetate:chloroform, 4:1 as an eluent to give oxametacyclophanes.

6,15-Dimethoxy-2,2-dimethyl-9,12-dioxatricyclo-[12.3.1.1^{3,7}]nonadeca-1(17),3(4),5,7(19),14(18),15-hexaene (**5**).

The yield of **5** was 44% as colorless crystals, mp 104-106°; ir (potassium bromide): 2958, 2925, 2870, 2839, 1606, 1500, 1461, 1360, 1295, 1244, 1192, 1143, 1118, 1081, 1031 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.70 (s, 6H, Me x 2), 3.41 (s, 4H, OCH$_2$ x 2), 3.82 (s, 6H, OMe x 2), 4.55 (s, 4H, ArCH$_2$O x 2), 6.82 (d, 2H, aromatic protons, J = 8.5 Hz), 7.07 (d, 2H, aromatic protons, J = 2.5 Hz), 7.39 (dd, 2H, aromatic protons, J = 2.5, 8.5 Hz); ^{13}C nmr (deuteriochloroform): δ 30.7, 42.3, 55.4, 67.0, 67.5, 109.4, 125.2 x 2, 131.1, 142.7, 155.5; fab-ms: m/z 343 (M+H)$^+$.

Anal. Calcd. for C$_{21}$H$_{26}$O$_4$: C, 73.66; H, 7.65. Found: C, 73.82; H, 7.72.

6,15,23,32-Tetramethoxy-9,12,26,29-tetraoxapentacyclo-[29.3.1.1^{3,7}.1^{14,18}.1^{20,24}]octatriaconta-1(34),3(4),5,7(36),14(37),15,17,20(21),22,24(38),31(35),32-dodecaene-2,19-dione (**6**).

The yield of **6** was 12% yield as colorless crystals, mp 201-205°; ir (potassium bromide): 2920, 2840, 1639, 1601, 1578, 1500, 1462, 1327, 1257, 1128, 1093, 1026, 827, 762 cm^{-1}; ^{1}H nmr (deuteriochloroform) : δ 3.70 (s, 8H, OCH$_2$ x 4), 3.87 (s, 12H, OMe x 4), 4.54 (s, 8H, ArCH$_2$ x 4), 6.95 (d, 4H, aromatic protons, J = 8.4 Hz), 7.78 (d, 4H, aromatic protons, J = 2.2 Hz), 7.80 (dd, 4H, aromatic protons, J = 2.2, 8.4 Hz); ^{13}C nmr (deuteriochlorofrom:DMSO-d$_6$, 4:1): δ 55.2, 66.9, 69.7, 109.5, 125.8, 129.8 x 2, 130.3, 159.3, 194.5; fab-ms: m/z 657 (M+H)$^+$.

Anal. Calcd. for C$_{38}$H$_{40}$O$_{10}$ H$_2$O: C, 67.64; H, 6.27. Found: C, 67.69; H, 6.03.

6,15-Dimethoxy-9,12-dioxatricyclo[12.3.1.1^{3,7}]nonadeca-1(17),3(4),5,7(19),14(18),15-hexaen-2-one (**7**).

The yield of **7** was 34% as colorless crystals, mp 244-249°; ir (potassium bromide): 2920, 2855, 1647, 1603, 1325, 1261, 1111, 1070, 1028, 920, 782 cm^{-1}; ^{1}H nmr (deuteriochlorofrom): δ 3.78 (s, 4H, OCH$_2$ x 2), 3.91 (s, 6H, OMe x 2), 4.68 (s, 4H, ArCH$_2$ x 2), 7.01 (d, 2H, aromatic protons, J = 8.6 Hz), 7.85 (d, 2H, aromatic protons, J = 2.4 Hz), 8.01 (dd, 2H, aromatic protons, J = 2.4, 8.6 Hz); ^{13}C nmr (deuteriochloroform): δ 55.3, 66.2, 68.4, 110.2, 124.5, 126.5, 129.6, 132.0, 159.8, 193.1; fab-ms: m/z 329 (M+H)$^+$.

Anal. Calcd. for C$_{19}$H$_{20}$O$_5$: C, 69.50; H, 6.14. Found: C, 69.42; H, 6.14.

35,36,37,38-Tetramethoxy-9,12,26,29-tetraoxa-5,16,22,33-tetrakis(*tert*-butyl)pentacyclo[29.3.1.1^{3,7}.1^{14,18}.1^{20,24}]octatriaconta-1(34),3(4),5,7(36),14(37),15,17,20(21),22,24(38),31(35),32-dodecaene (**8**).

The yield of **8** was 3% yield as colorless crystals, mp 204-205°; ir (potassium bromide): 2960, 2904, 2865, 2831, 1602, 1483, 1463, 1432, 1392, 1363, 1296, 1245, 1209, 1139, 1105, 1051, 1012, 1002 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.20 (s, 36H, *t*-Bu x 4), 3.39 (s, 12H, OMe x 4), 3.70 (s, 8H, OCH$_2$ x 4), 3.93 (s, 4H, ArCH$_2$Ar x 2), 4.52 (s, 8H, ArCH$_2$O x 4), 7.04 (d, 4H, aromatic protons, J = 2.5 Hz), 7.21 (d, 4H, aromatic protons, J = 2.5 Hz); ^{13}C nmr (deuteriochloroform): δ 30.4, 31.4, 34.2, 61.6, 68.9, 69.7, 125.6, 127.9, 130.2, 133.1, 146.2, 154.7; ei-ms (70 eV): m/z 852 (M)$^+$.

Anal. Calcd. for C$_{54}$H$_{76}$O$_8$: C, 76.02; H, 8.98. Found: C, 76.31; H, 9.27.

Synthesis of 6-(*tert*-butyl)-4-(1-(5-(*tert*-butyl)-4-hydroxy-3-(hydroxymethyl)phenyl)isopropyl)-2-(hydroxymethyl)phenol (**18**).

To a solution of **10b** (8.0 g, 25 mmoles), 20% KOH aqueous solution (160 ml), methanol (120 ml) was added a solution of 18% formalin (86 g, 510 mmoles) over 3 hours at 45° under nitrogen atmosphere. After the addition was complete, the mixture was stirred for 1.5 hours at 45°. The mixture was acidified by 10% HCl aqueous solution until *p*H 1, and then the resulting precipitates were extracted with ethyl acetate (70 ml) 4 times. The organic layer was washed with water until neutral, and then dried over anhydrous sodium sulfate. Removal of ethyl acetate gave a pale yellow oily residue, which was subjected to column chromatography on silica gel using ethyl acetate:hexane, 2:5 as an eluent to give colorless crystals, which was recrystallized from hexane-ethyl acetate to give **18** (5.7 g, 55% yield) as colorless crystals, mp 160-162°; ir (potassium bromide): 3496, 3434, 3369, 2962, 2869, 1608, 1479 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.37 (s, 18H, *t*-Bu x 2), 1.61 (s, 6H, Me x 2), 2.04 (t, 2H, OH x 2, J = 5.7 Hz), 4.80 (d, 4H, CH$_2$ x 2, J = 5.7 Hz), 6.71 (d, 2H, Ar-H x 2, J = 2.2 Hz), 7.10 (d, 2H, Ar-H x 2, J = 2.2 Hz),

7.55 (s, 2H, Ar-OH x 2); ^{13}C nmr (deuteriochloroform): δ 29.7, 31.2, 34.9, 41.9, 65.7, 123.9, 124.1, 125.4, 136.2, 141.3, 153.1; fab-ms: m/z 401 $(M+H)^+$.

Anal. Calcd. for $C_{25}H_{36}O_4$: C, 74.96; H, 9.06. Found: C, 75.13; H, 9.23.

Synthesis of 2-(*tert*-butyl)-4-(1-(5-(*tert*-butyl)-3-(chloromethyl)-4-hydroxyphenyl)isopropyl)-6-(chloromethyl)phenol (**19**).

To a solution of **18** (416 mg, 1.0 mmole) in dry benzene (10 ml) was added a solution of thionyl chloride (0.29 ml, 4.0 mmoles) in dry benzene (5 ml) at room temperature over 20 minutes. After the addition was complete, the mixture was stirred at room temperature for 3 hours. Removal of benzene and excess thionyl chloride under reduced pressure gave colorless powder, which was washed with hexane. Recrystallization of the powder from benzene gave pure **19** (407 mg, 90% yield) as white powder, mp 82-86°; ir (potassium bromide): 3542, 3399, 2962, 2869, 1606, 1479 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.36 (s, 18H, *t*-Bu x 2), 1.63 (s, 6H, Me x 2), 4.66 (s, 4H, CH_2 x 2), 5.42 (s, 2H, Ar-OH x 2), 6.93 (d, 2H, Ar-H x 2, J = 1.0 Hz), 7.13 (d, 2H, Ar-H x 2, J = 1.0 Hz); ^{13}C nmr (deuteriochloroform): δ 29.8, 31.1, 34.8, 42.1, 44.9, 123.0, 126.1, 127.0, 136.9, 142.2, 151.7; fab-ms: m/z 401 $(M-Cl)^+$.

Anal. Calcd. for $C_{25}H_{34}Cl_2O_2$: C, 68.64; H, 7.83. Found: C, 68.45; H, 7.89.

General Procedure for the Preparation of the Macrocycles (**9**).

To a suspension of sodium carbonate (424 mg, 4.0 mmoles) in dimethylformamide (20 ml) were added a solution of amine derivative (1.0 mmole) in dimethylformamide (15 ml) and a solution of **19** (401 mg, 1.0 mmole) in dimethylformamide (15 ml) at room temperature over 1 hour. After the addition was complete, the mixture was allowed to stir at room temperature for 5 hours. Removal of dimethylformamide under reduced pressure gave a yellow oily residue, which was subjected to column chromatography on silica gel to give **9** as colorless powders.

9,23-Diaza-9,23-bisbenzyl-2,2,16,16-tetramethyl-5,13,19,27-tetrakis(*tert*-butyl)pentacyclo[23.3.1.1^{3,7}.1^{11,15}.1^{17,21}]dotriaconta-1(28),3(4),5,7(30),11(12),13,15(31),17(18),19,21(32),25(29),26-dodecaene-6,12,20,26-tetraol (**9a**).

The yield of **9a** was 40% as colorless crystals, mp 250-251°; ir (chloroform): 3546, 2964, 2911, 2869, 1602, 1477 cm^{-1}; ^{1}H nmr (deuteriochloroform at -60°): δ 1.43 (s, 18H, *t*-Bu_1 x 2), 1.49 (s, 24H, *t*-Bu_2 x 2 and Me_2 x 2), 1.56 (s, 6H, Me_1 x 2), 2.63 (d, 2H, H_a, J = 13.5 Hz), 2.87 (d, 4H, H_c and H_e, J = 13.5 Hz), 3.79 (d, 2H, H_d, J = 13.5 Hz), 3.95 (d, 2H, H_b, J = 13.5 Hz), 4.00 (d, 2H, H_f, J = 13.5 Hz), 5.17 (br s, 2H, OH_1 x 2), 6.19 (s, 2H, H_h x 2), 6.34 (s, 2H, H_i x 2), 7.30 (s, 2H, H_j x 2), 7.33 (s, 2H, H_g), 7.36-7.47 (m, 10H, Ph x 2), 9.28 (br s, 2H, OH_2 x 2); ^{1}H-^{1}H roesy (deuteriochloroform, mixing time = 0.3 second at -60°): c/d; a/b; e/f; *t*-Bu_1/g; *t*-Bu_2/j; d/OH_2; Ph/OH_2; Ph/OH_1; e/Ph; f/Ph; c/i; d/i; f/i; a/h; d/h; b/h; b/OH_1; a/OH_1; a/d; Me_1/h; Me_2/h; Me_1/i; Me_2/i; *t*-Bu_1/Ph; ^{13}C nmr (deuteriochloroform): δ 29.9, 31.6, 35.2, 42.7, 56.8, 58.7, 122.0, 123.2, 128.2, 129.3, 129.7, 135.0, 137.8, 142.7, 152.0; fab-ms: m/z 943 $(M+H)^+$.

Anal. Calcd. for $C_{64}H_{82}N_2O_4$: C, 81.49; H, 8.76; N, 2.97. Found: C, 81.62; H, 9.01; N, 3.15.

9,23-Diaza-9,23-bis((1*S*)-1-(methoxycarbonyl)-2-methylpropyl)-2,2,16,16-tetramethyl-5,13,19,27-tetrakis(*tert*-butyl)pentacyclo[23.3.1.1^{3,7}.1^{11,15}.1^{17,21}]dotriaconta-1(28),3(4),5,7(30),11(12),13,15(31),17(18),19,21(32),25(29),26-dodecaene-6,12,20,26-tetraol (**9b**).

The yield of **9b** was 15% as colorless crystals, mp 192-198°; $[\alpha]_D^{20}$ = -46° (c = 0.1, chloroform); ir (chloroform): 3689, 3397, 2964, 2910, 2869, 1722, 1602, 1477 cm^{-1}; ^{1}H nmr (deuteriochloroform at -60°): δ 0.80 (d, 3H, Me_3, J = 6.0 Hz), 0.91 (d, 3H, Me_1, J = 6.0 Hz), 0.93 (d, 3H, Me_2, J = 6.0 Hz), 1.19 (d, 3H, Me_4, J = 6.0 Hz), 1.37 (s, 9H, *t*-Bu_1), 1.42 (s, 9H, *t*-Bu_3, 9H), 1.50 (s, 9H, *t*-Bu_2), 1.53 (s, 15H, *t*-Bu_4 and Me_a x 2), 1.61 (s, 6H, Me_b x 2, 6H), 2.24 (m, 1H, H_s), 2.32 (m, 1H, H_t), 2.71 (d, 1H, H_e, J = 14.0 Hz), 2.93 (d, 1H, H_r, J = 10.5 Hz), 2.94 (d, 1H, H_c, J = 13.0 Hz), 3.02 (d, 1H, H_a, J = 14.5 Hz), 3.05 (d, 1H, H_g, J = 13.0 Hz), 3.45 (s, 1H, H_q), 3.60 (d, 1H, H_f, J = 14.0 Hz), 3.67 (d, 1H, H_b, J = 14.5 Hz), 3.71 (s, 3H, CO_2Me_2), 3.82 (s, 3H, CO_2Me_1), 4.28 (d, 1H, H_h, J = 13.0 Hz), 4.31 (d, 1H, H_d, J = 13.0 Hz), 5.78 (br s, 1H, OH_3), 6.07 (s, 1H, H_k), 6.12 (s, 1H, H_j), 6.27 (s, 1H, H_p), 6.34 (s, 1H, H_m), 7.25 (s, 1H, H_n), 7.26 (s, 1H, H_i), 7.37 (s, 1H, H_o), 7.39 (s, 1H, H_l), 8.52 (br s, 1H, OH_4), 8.54 (s, 1H, OH_2), 8.88 (s, 1H, OH_1); ^{1}H-^{1}H roesy (deuteriochloroform, mixing time = 0.3 second at -60°): b/OH_1; q/OH_1; d/OH_2; c/OH_2; *t*-Bu_4/OH_4; Me_4/OH_4; Me_b/l; t-Bu_2/l; *t*-Bu_4/o; *t*-Bu_1/i; Me_a/i; *t*-Bu_3/n; k/m; b/m; f/m; e/m; Me_b/m; j/p; h/p; f/p; e/p; Me_a/p; b/j; q/j; a/j; Me_a/j; d/k; b/d; c/k; Me_a/k; h/OH_3; f/OH_3; r/OH_3; *t*-Bu_2/OH_3; Me_4/OH_3; c/d; Me_1/d; g/h; t/h; Me_1/CO_2Me_1; Me_3/CO_2Me_2; a/b; s/b; e/f; a/q; c/q; s/q; Me_2/q; e/g; t/g; s/a; s/c; Me_4/r; Me_3/r; r/e; Me_4/t; Me_3/t; Me_1/s; Me_2/s; ^{13}C nmr (deuteriochloroform at 55°): δ 19.9, 25.7, 29.8, 31.0, 34.9, 42.4, 51.2, 53.0, 121.7, 123.0, 130.0, 135.0, 142.5, 152.3, 173.8; fab-ms: m/z 992 $(M+H)^+$.

Anal. Calcd. for $C_{62}H_{90}N_2O_8$: C, 75.11; H, 9.15; N, 2.83. Found: C, 75.35; H, 9.32; N, 2.61.

9,23-Diaza-9,23-bis((1*S*)-2-(4-hydroxyphenyl)-1-(methoxycarbonyl)ethyl)-2,2,16,16-tetramethyl-5,13,19,27-tetrakis(*tert*-butyl)pentacyclo[23.3.1.1^{3,7}.1^{11,15}.1^{17,21}]dotriaconta-1(28),3(4),5,7(30),11(12),13,15(31),17(18),19,21(32),25(29),26-dodecaene-6,12,20,26-tetraol (**9c**).

The yield of **9c** was 32% as colorless crystals, mp 188-190°; $[a]_D^{20}$ = -25° (c = 0.1, chloroform); ir (chloroform): 3689, 3586, 3400, 2958, 2910, 2869, 1724, 1602, 1477 cm^{-1}; ^{1}H nmr (deuteriochloroform at -40°): δ 1.33 (s, 9H, *t*-Bu_1), 1.42 (s, 9H, *t*-Bu_2), 1.48 (s, 9H, *t*-Bu_4), 1.50 (s, 9H, *t*-Bu_3), 1.53 (s, 6H, Me x 2), 1.56 (s, 3H, Me), 1.61 (s, 3H, Me), 2.59 (br s, 1H, H_a), 2.93 (d, 1H, H_g, J = 13.5 Hz), 2.95 (d, 1H, H_e, J = 13.0 Hz), 3.00 (dd, 2H, H_s and H_t, J = 8.5, 14.0 Hz), 3.23 (d, 1H, H_c, J = 13.0 Hz), 3.30 (dd, 2H, H_u and H_v, J = 8.0, 14.0 Hz), 3.52 (d, 1H, H_b, J = 14.0 Hz), 3.60 (d, 1H, H_h, J = 13.5 Hz), 3.64 (s, 3H, CO_2Me), 3.70 (s, 3H, CO_2Me), 3.75 (dd, 2H, H_q and H_r, J = 8.5, 12.5 Hz), 4.05 (d, 1H, H_f, J = 13.0 Hz), 4.29 (d, 1H, H_d, J = 13.0 Hz), 5.09 (br s, 2H, OH x 2), 5.98 (s, 1H, H_m), 6.07 (s, 1H, H_j), 6.25 (s, 1H, H_k), 6.29 (s, 1H, H_p), 6.51 (br s, 2H, aromatic protons of tyrosine residue), 6.74 (br s, 2H, aromatic protons of tyrosine residue), 6.84 (d, 2H, aromatic protons of tyrosine residue, J = 8.0 Hz), 7.10 (d, 2H, aromatic protons of tyrosine residue, J = 8.0 Hz), 7.24 (s, 1H, H_i), 7.30 (s, 1H, H_o), 7.37 (s, 1H, H_n), 7.40 (s, 1H, H_l), 8.27 (s, 1H, OH), 8.73 (s, 1H, OH,); ^{1}H-^{1}H roesy (deuteriochloroform, mixing time = 0.3 second at -40°): *t*-Bu_1/i; *t*-Bu_2/l; *t*-Bu_3/o; *t*-Bu_4/n; k/d; k/h; j/a; j/h; m/b; m/e; p/g; p/b; c/a; c/d; c/t; c/v; f/r; q/d; h/g; b/a; b/d; s/u; t/v; ^{13}C nmr (deuteriochloroform at 55°): δ 29.8, 31.1, 33.1, 35.0, 42.4, 51.4, 52.5, 61.6, 115.6, 121.2, 123.2, 129.4, 129.9, 130.3, 135.3, 142.2, 152.3, 154.6; fab-ms: m/z 1120 $(M+H)^+$.

Anal. Calcd. for $C_{70}H_{90}N_2O_{10}$: C, 75.10; H, 8.10; N, 2.50. Found: C, 74.98; H, 7.90; N, 2.43.

9,23-Diaza-9,23-bis((1*R*)-1-phenylethyl)-2,2,16,16-tetramethyl-5,13,19,27-tetrakis(*tert*-butyl)pentacyclo[23.3.1.1^{3,7}.1^{11,15}.1^{17,21}]-dotriaconta-1(28),3(4),5,7(30),11(12),13,15(31),17(18),19,21(32),25(29),26-dodecaene-6,12,20,26-tetraol (**9d**).

The yield of **9d** was 50% as colorless crystals, mp 79-82°; $[\alpha]_D^{20}$ = +23° (c = 0.1, chloroform); ir (chloroform): 3520, 3311, 2964, 2929, 2869, 1602, 1477 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.37 (s, 36H, *t*-Bu x 4), 1.43 (d, 6H, Me x 2, J = 6.0 Hz), 1.55 (s, 12H, Me x 4), 3.65 (d, 4H, methylene protons, J = 13.5 Hz), 3.74 (d, 4H, methylene protons, J = 13.5 Hz), 3.77 (q, 2H, methine protons, J = 6.0 Hz), 6.57 (d, 4H, aromatic protons, J = 2.0 Hz), 7.04 (d, 4H, aromatic protons, J = 2.0 Hz), 7.20-7.35 (m, 10H, Ph x 2); ^{1}H-^{1}H roesy (deuteriochloroform, mixing time = 0.3 second at 20°): *t*-Bu/e; Me_1/Ph; a/d; b/d; c/Ph; d/Me_2; e/Me_2; ^{13}C nmr (deuteriochloroform): δ 23.2, 29.6, 31.2, 34.8, 41.7, 51.2, 57.3, 122.1, 124.3, 124.9, 126.5, 127.4, 128.7, 135.5, 140.5, 143.6, 154.4; fab- ms:m/z 972 $(M+H)^+$.

Anal. Calcd. for $C_{62}H_{90}N_2O_8$: C, 75.11; H, 9.15; N, 2.83. Found: C, 75.28; H, 9.25; N, 2.68.

T_1 Measurements.

The T_1 values were obtained in deuteriochloroform at 24° by using an inversion recovery method. The nmr samples were sealed under vacuum after degassing by five freeze-pump-thaw cycles. The T_1 vaules for protons showed good responsibility with in 5% relative standard deviation.

Solvent Extraction.

Solvent extraction was carried out according to Pedersen's method. The dichloromethane solution (5 ml) containing the macrocycle (7 x 10^{-4} *M*) and the aqueous solution (5 ml) containing the metal nitrate (1 x 10^{-1} *M*) and picric acid (7 x 10^{-5} *M*) were mixed and shaken for 10 minutes at 25°. The solution was equilibrated. Extraction of the picrate was followed by monitoring the absorbance of the aqueous solution at 354 nm.

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